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EXAMINER	
ORWIG, KEVIN S	
ART UNIT	PAPER NUMBER
1611	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

DocketingDept@young-thompson.com

Office Action Summary	Application No.	Applicant(s)	
	10/575,449	ROYERE ET AL.	
	Examiner	Art Unit	
	Kevin S. Orwig	1611	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28,29 and 31-55* is/are pending in the application.

4a) Of the above claim(s) *49-54* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,29,31-48 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendments and arguments filed Apr. 29, 2010 are acknowledged and have been fully considered. Claims 28, 29, 31-55 are now pending. Claims 1-27 and 30 are cancelled; claims 28, 31, 34, and 47 are amended; claims 49-54 are withdrawn; claim 55 has been added. Claims 28, 29, 31-48, and 55 are now under consideration.

OBJECTIONS/REJECTIONS WITHDRAWN

The objection to claim 47 is withdrawn in light of the claim amendments.

OBJECTIONS/REJECTIONS MAINTAINED

The rejection of claims 28, 29, 31-33, and 36-48 under 35 U.S.C. 103(a) over JANSEN, WESTESEN, and MONDAIN-MONVAL is maintained as discussed below.

The rejection of claims 28, 29, 31-33, and 36-48 under 35 U.S.C. 103(a) over JANSEN, WESTESEN, MONDAIN-MONVAL, and RABUSSIER is maintained as discussed below.

The rejection of claims 28, 29, 31-33, and 36-48 under 35 U.S.C. 103(a) over BIBETTE, WO 99/07463, and NAKAMURA is maintained as discussed below.

The rejection of claims 29, 40, 42, 43, 47, and 48 under 35 U.S.C. 103(a) over BIBETTE, WO 99/07463, NAKAMURA, LIN, and KRAFFT is maintained as discussed below.

Claim Rejections - 35 USC § 103 (Maintained)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 28, 29, 31-33, and 36-48 are rejected under 35 U.S.C. 103(a) as being unpatentable over JANSEN (U.S. 2004/0071716; Filed Feb. 20, 2002) in view of WESTESEN (U.S. 6,207,178; Issued Mar. 27, 2001) and MONDAIN-MONVAL (WO 01/33223; Published May 10, 2001) as evidenced by U.S. 6,866,838.

Since the WO document to Mondain-Monval is in French, the '838 Patent, which is the result of the national stage entry of the international application, is relied upon as an English language equivalent. Column and line numbers refer to the '838 Patent.

1. Jansen discloses water-in-oil-in-water (w/o/w) emulsions comprising adjuvants or therapeutical (i.e. active) agents and stabilizing agents (abstract; par. [0044]). These emulsions contain a dispersed water-in-oil (w/o) phase (i.e. a lipid phase) in a continuous aqueous phase (example 3). Jansen teaches the use of emulsifiers (i.e. stabilizing agents), including PEG-30 dipolyhydroxystearate (i.e. Arlacel P135), which comprises two fatty acid chains and one polyethylene glycol (PEG) chain of 30 polyethylene glycol units (examples 1-6). The dispersed lipid phase droplets in these emulsions are from 1-5 μm (example 3), which is considered monodisperse according to the instant specification (pars. [0029] and [0039]). Jansen does not teach the use of lipids that are crystallizable as defined in the instant specification.

2. However, Westesen discloses suspensions of solid lipid particles, which are oil-in-water emulsions of dispersed lipid phase particles in a continuous water phase (abstract; examples 1-3). The lipid particles (i.e. the lipid phase) taught by Westesen

form matrices that carry bioactive agents (col. 10, lines 20-67). The solid lipid particles are made of fats including di- and tri-glycerides of long chain fatty acids that are solid at room temperature (i.e. crystallizable lipids) (col. 5, lines 23-26; col. 9, lines 20-29). It is noted that the crystallizable lipids may be tripalmitate, a saturated C_{16} fatty acid derivative.

3. Moreover, Mondain-Monval discloses compositions comprising nanospheres (of up to 1 μm) for drug delivery (abstract; col. 3, lines 1-5; col. 4, lines 35-42; col. 5, lines 1-15). Mondain-Monval teaches that such particles advantageously have a narrow particle size distribution (i.e. are monodisperse or isodisperse) (col. 1, lines 56-58). Mondain-Monval teaches how to make monodispersed compositions (col. 5, line 66 to col. 6, line 9; Example 1). In light of these teachings, it would have been *prima facie* obvious for an artisan to specifically make monodispersed compositions and the artisan would have been aware of how to do so.

4. Jansen teaches that an improvement over the prior art is to provide emulsions that are stable (abstract; pars. [0010], [0030], and [0037]), have utility in parenteral administration (pars. [0030] and [0049]) and have utility as vaccines (abstract; pars. [0001], [0012], and [0040]). Westesen teaches that the compositions are extremely stable (col. 12, lines 18-19; claim 1) and that they are useful as delivery systems for a variety of administration routes including, *inter alia*, parenteral (e.g. intravenous), nasal, and pulmonary administration as well as useful as vaccines (abstract; col. 1, line 60 to col. 2, line 12; col. 5, lines 27-32). It is clear that difficulties in obtaining stable, fluid emulsions for the administration routes discussed above were recognized in the art and

addressed by both Jansen and Westesen. In light of these teachings, the skilled artisan would have been motivated to include crystallizable lipids in the composition taught by Jansen with the expectation of producing a stable emulsion for the delivery of lipophilic active agents in the oil phase, which would be useful for a variety of administration routes. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to substitute known crystallizable lipid components as taught by Westesen in the emulsions of Jansen to prepare a monodispersed drug delivery system with the expected result of solving the same problem, reading on instant claims 28, 30, 33, 36, and 37.

5. Instant claim 29 recites the composition of claim 28 in which an inner aqueous phase is dispersed in the dispersed lipid phase. In this situation, the composition is a water-in-oil-in-water (w/o/w) emulsion. Jansen teaches w/o/w emulsions in which an "inner" aqueous phase is dispersed in an oil phase comprising Miglyol 840, which is in turn dispersed in another aqueous phase (example 3), reading on instant claim 29.

6. Westesen teaches that the lipid phase of their compositions may be approximately 11% by weight relative to the total composition weight (see example 2, where 7.84 g lipid phase is dispersed in water to a total weight of 70 g), which is within the range of 0.01-30% by weight, reading on instant claim 31.

7. Jansen teaches the use of Arlacel P135 (i.e. the stabilizing agent) at 3% by weight, which is within the range of 0.001-30% by weight, reading on instant claim 32.

8. The aqueous phases of the emulsions taught by Jansen contain antigens and phosphate buffered saline (PBS) (i.e. a salt). Since PBS contains sodium chloride, it is

considered a cryoprotective agent as defined in the instant specification (paragraph [0046]) (example 3), reading on instant claims 38 and 39.

9. Jansen teaches that the bioactive agents may be antigens (i.e. proteins) that are present in the inner water phase. Furthermore, the lipid particles taught by Westesen form matrices that carry bioactive agents (col. 10, lines 20-67). These bioactive agents may be pharmaceutical active principles (col. 10, lines 32-60; col. 14, line 58 to col. 15, line 27), such as, *inter alia*, antibiotics (i.e. antibacterial agents), beta blockers, and vitamins (col. 10, lines 32-60). Westesen also teaches that the bioactive agents may be angiotensin converting enzyme (ACE) inhibitors (col. 10, line 40). Since ACE is an exopeptidase, it is a protease. ACE inhibitors are thus protease inhibitors, reading on instant claims 44-48.

10. Westesen teaches that their compositions may comprise mixtures of bioactive agents (abstract; col. 15, lines 52-53). Thus, these compositions can contain at least two active principles, reading on instant claim 40.

11. In the case of the w/o/w emulsion taught by Jansen (example 3) the lipid phase (i.e. the dispersed w/o emulsion) contains a water soluble active principle (the antigen compounds), reading on instant claim 41.

12. Westesen teaches the use of both water soluble compounds (col. 10, lines 26-31) and sparingly water soluble compounds (col. 14, lines 54-62) as bioactive agents. Westesen also teaches that their compositions may comprise mixtures of bioactive agents as described above in paragraph 10. Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include both a

water soluble active principle and a sparingly water soluble active principle in the lipid phase of the emulsions taught by Jansen as needed to produce a drug delivery system to treat multiple conditions or to deliver multiple drugs for the same condition, reading on instant claims 42 and 43.

Response to Arguments

Applicants' arguments have been fully considered but are not persuasive. Applicants broadly assert that a skilled artisan combining Jansen and Westesen would add the "adjuvants" described in Jansen, which applicants assert are excluded by the new "consisting of" language (response, p. 12).

Applicants fail to point to any example of a compound required in Jansen's lipid phase that would be excluded by the instant "consisting of" language. The term "adjuvant" as used by Jansen refers to the overall compositions, not to certain compounds required therein (see, e.g. the abstract). Moreover, rather than being excluded, the compound(s) referred to by applicant is a block copolymer that meets the instant requirements of a compound stabilizing the dispersed phase comprising two fatty acid chains and one PEG chain (see pars. [0012]-[0031], cited by applicants). Applicants are invited to explain how the instant claim language excludes such a copolymer which comprises a PEG chain and at least two fatty acid chains.

Applicants argue that a declaration has previously been filed regarding alleged disadvantages of the prior art (response, p. 12).

The deficiencies of the declaration (filed 10/19/09, referred to by applicants) have been addressed previously (see pgs. 10-12 of the Office Action dated 2/3/10). The

declaration is not considered persuasive.

Claims 28, 34, 35, and new claim 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jansen, Westesen, and Mondain-Monval as applied to claims 28-33 and 36-48 above in further view of RABUSSIER (U.S. 3,258,326; Issued Jun. 28, 1966).

13. The composition of instant claim 28 is taught by Jansen and Westesen as applied above. Neither Jansen nor Westesen teaches the use of a thickener or alginic acid salts.

14. However, the use of alginates as components in emulsions is well-known. For instance, Rabussier discloses formulations comprising stable oil-in-water emulsions (col. 2, line 31) and hydrophilic colloids (col. 2, lines 25-28) for delivery of active agents (col. 2, lines 19-22). The hydrophilic colloids taught by Rabussier may be alginates that are added to the water (i.e. the aqueous phase) to maintain stability of the suspension (col. 1, lines 34-42; col. 3, lines 63-72; claim 7). Furthermore, Rabussier teaches that the alginate may be used in 0.2% by weight (example 4). Since alginates were known in the art in the instantly claimed weight % range, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to include this known component as a stabilizer in the composition taught by of Jansen and Westesen to prepare a more stable drug delivery system, reading on instant claims 34 and 35.

Response to Arguments

Applicants' arguments have been addressed *supra*, and that discussion is

incorporated herein. No further arguments were presented regarding Rabussier.

Claims 28, 29, 31-39, 41, and 44-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over BIBETTE (WO 01/021297; Published Mar. 29, 2001) in view of WO 99/07463; Published Feb. 18, 1999 (hereinafter '463) and NAKAMURA (WO 02/074260; Published Sep. 26, 2002), as evidenced by U.S. 7,214,717, U.S. 6,627,603, and U.S. 2004/0137019.

Since the WO documents to Bibette and Nakamura are in languages other than English (i.e. French and Japanese), the '717 and '603 Patents (to Bibette) and the '019 pre-grant publication (to Nakamura), which are the result of the respective national stage entries of the international applications, are relied upon as English language equivalents. Column, line, and paragraph numbers refer to the '717 or '603 Patents or the '019 application publication as appropriate. It is further noted that the primary and one of the secondary references applied are the work of one of the instant inventors, yet neither was provided to the Office on any IDS.

15. Bibette discloses monodisperse stable double w/o/w emulsions and methods of their preparation (title; abstract), and teaches that the compositions are advantageous for pharmaceuticals and/or cosmetics because of the ability to control release kinetics of agents contained in the emulsions (col. 1, lines 9-21). Bibette teaches the double emulsions are composed of a monodisperse inverse emulsion dispersed in an aqueous external phase, the inverse emulsion itself being composed of droplets of an aqueous internal phase dispersed in an oily phase and defines "monodisperse" in substantially the same way as the instant application (col. 1, lines 62-67; col. 2, lines 20-25; col. 7,

lines 9-13; col. 8, lines 45-48; Example 1). Bibette teaches that the inner aqueous phase (i.e. internal to the lipid phase) preferably comprises an active substance (abstract; col. 1, lines 16-18; col. 5, lines 25-26). Thus, the lipid phase overall comprises an active substance. Bibette teaches how to control the size of the lipid globules of the lipid phase emulsion (col. 1, lines 38-43; col. 7, lines 60-63) and states that the dispersed lipid globules have a size notably between 2-10 μm (col. 8, lines 45-48; Examples 1 and 4; Figs. 2-4). Bibette teaches that the nature of the oily phase is not determinant in the invention and that the nature of the oil components is not critical (col. 4, lines 42-43; col. 5, lines 8-9). Bibette does not explicitly teach the use of crystallizable lipids. Bibette only discloses the use of one class of surfactant for the oily phase, namely polyglycerol polyricinoleate. However, the use of the crystallizable lipids and other surfactant components would have been obvious to a skilled artisan.

16. For example, '463 (also to Bibette) discloses monodisperse multiple w/o/w emulsions containing at least one active principle and solubilized by a surfactant (abstract). Bibette teaches fat soluble surfactants such as polyglycerol polyricinoleate and polyalkylene dipolyhydroxystearates (i.e. a stabilizer comprising two fatty acid chains and one polyethylene glycol chain (col. 5, lines 17-18). Thus, '463 teaches an overlapping set of surfactants to that of Bibette and establishes the functional equivalence of the surfactants taught by Bibette and those instantly claimed.

17. Moreover, Nakamura discloses stable w/o/w emulsions that can carry active agents such as cosmetics, vitamins, and drugs (abstract; pars. [0013]-[0016]). Nakamura teaches that the oil phase is not particularly limited and can contain a liquid

or solid oil component or mixtures thereof (pars. [0019] and [0028]). Nakamura teaches solid fats or waxes, any of which meets the definition of a crystallizable lipid in the instant specification (pars. [0021]-[0022]). Nakamura teaches glyceryl triisopalmitate (i.e. tripalmitin), a saturated C_{16} fatty acid derivative. In line with the teachings of '463, Nakamura teaches that the internal aqueous phase and oil phase are emulsified with an emulsifier having an HLB value of not more than 7, since using emulsifiers with higher HLB values does not give stable emulsions (par. [0029]). Nakamura teaches that particularly preferred emulsifiers include polyethyleneglycol dipolyhydroxystearate (i.e. Arlacel P135, which comprises two fatty acid chains and one polyethylene glycol (PEG) chain of 30 polyethylene glycol units) (par. [0032]).

18. In light of these teachings, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to utilize a solid (i.e. crystallizable) lipid in the w/o/w emulsions of Calderon. Based on Nakamura's teachings, doing so represents substitution of one known element for another to obtain predictable results. It would also have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used an equivalent surfactant, such as those taught by '463, particularly since Nakamura teaches that this surfactant is preferable to prepare stable w/o/w emulsions. Claims 28, 29, 33, 36, 37, and 41 are rendered obvious by Bibette, '463, and Nakamura.

19. Bibette teaches that the lipid phase can be less than 20% by weight (see Example 1), given the proportion of aqueous phase present in the oily phase. Also, Nakamura exemplifies w/o/w emulsions having between 0.01-30% wt. of the lipid phase

(e.g. Tables I-III, Examples 8 and 9). Bibette teaches that the quantity of surfactants depends on the nature of the surfactant as well as the other constituents present and can be determined by a person skilled in the art (col. 3, lines 59-63). Further, Nakamura teaches that the amount of the emulsifier having an HLB value of 7 or less is preferably 0.01-10% by weight (par. [0033]). Thus, selecting such amounts would be mere routine optimization for a skilled artisan. Claims 31 and 32 are rendered obvious by Bibette, '463, and Nakamura.

20. Bibette teaches the use of a polysaccharide thickening agent, in an amount of 1-10 % wt., and teaches that alginates are the preferred thickening agents (abstract; col. 3, lines 1-17). Claims 34 and 35 are rendered obvious by Bibette, '463, and Nakamura.

21. Bibette teaches that the aqueous continuous phase preferably comprises osmotic pressure balancing agents such as sorbitol, glycerol, or various salts (col. 4, lines 3-14) (i.e. cryoprotective agents as defined in the instant specification). Claims 38 and 39 are rendered obvious by Bibette, '463, and Nakamura.

22. The teachings of Bibette, '463, and Nakamura are presented *supra*. Regarding the recitations of certain active agents, applicants are advised that the mere recitation of a particular active agent, without more, will not result in patentably distinguishing the claimed invention from the prior art. Bibette teaches that any type of active substance generally used in one or more of the pharmaceutical, cosmetic, pest and disease control, or food fields can be used in the invention. Bibette teaches these agents can be, *inter alia*, vitamins (i.e. nutrients), vaccines, anti-inflammatory agents, and anti-

cancer agents, and preservatives (col. 5; lines, 29-39). Claims 44-46 are rendered obvious by Bibette, '463, and Nakamura.

Response to Arguments

Applicants' arguments have been fully considered but are not persuasive.

At the outset, it is noted that applicants have not responded to the issue of the lack of disclosure of the Bibette references WO 01/021297 and WO 99/07463, which are the work of one of the instant inventors, but were not provided to the USPTO.

Applicants argue that polyglycerol polyricinoleate does not read on the instant stabilizing compound (response, p. 14).

First, applicants provide no reasoning to support this assertion, and it is unclear how polyglycerol polyricinoleate does not read on the broad genus of compounds comprising two fatty acid chains and one polyethylene glycol chain. Second, and more importantly, polyglycerol polyricinoleate was not stated to read on applicants' claimed stabilizing compound. Rather, polyethyleneglycol dipolyhydroxystearate (i.e. Arlacel P135) (taught by Bibette ('463) and Nakamura) meets this limitation (see pars. 16 and 17 of the Office Action dated 2/3/10). It is noted that applicants ignore the teachings of Nakamura in making this argument. In response to applicants' arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Applicants assert that the prior art references teach a monodispersed internal

aqueous phase, not a monodisperse lipid phase (response, p. 15).

The examiner cannot agree. Again, in making this assertion, applicants do not support it in any way, in particular failing to point to any portion of the cited prior art documents that would support their position. In contrast, the examiner has pointed to evidence in the prior art that directly contradicts applicants' assertion. For example, see Bibette at col. 1, lines 62-67; col. 2, lines 20-25; col. 7, lines 9-13; col. 8, lines 45-48; Example 1. See also col. 7, lines 60-63, where Bibette teaches that it is the droplets of the internal emulsion E_i (i.e. the oil phase), that have a very narrow granulometric distribution. Thus, applicants' unsupported assertion is unpersuasive.

Claims 29, 40, 42, 43, 47, 48, and new claim 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bibette in view of '463 and Nakamura, as applied to claims 28, 29, 31-39, 41, 44-46 above, and further in view of LIN (U.S. 5,948,855; Issued Sep. 7, 1999) and KRAFFT (U.S. 5,980,936; Issued Nov. 9, 1999).

23. The teachings of Bibette, '463, and Nakamura are presented *supra*. While Bibette only teaches an active agent in the internal aqueous phase, the use of active agents in any phase of the emulsion is no more than an obvious variation.

24. For example, Lin discloses w/o/w multiple emulsions in which vitamins or drugs can be included in either the oil or aqueous phase (abstract; col. 2, lines 5-19). Additionally, Krafft discloses multiple emulsions that for the delivery of various drugs and therapeutic agents (abstract; col. 3, lines 35-36). It is an object of the invention to deliver both lipophilic and hydrophilic compounds in a controlled way (col. 3, lines 9-12). Krafft teaches that both lipophilic and hydrophilic agents are advantageously delivered,

preferably water soluble bioactive agents are delivered in combination with a lipophilic or hydrophobic agent (col. 6, lines 51-57). In light of these teachings, it would have been *prima facie* obvious for an artisan to include both a hydrophilic and a hydrophobic agent in the compositions of Bibette since the artisan would recognize the advantages and efficiency of simultaneous drug delivery. Moreover, Krafft teaches a set of bioactive agents overlapping that of Bibette, and the set taught by Krafft includes ACE inhibitors (i.e. protease inhibitors) (col. 13, lines 52-66). Claims 40, 42, 43, 47, and 48 are rendered obvious by Bibette, '463, Nakamura, Lin, and Krafft.

Regarding the obviousness rejections herein, it is noted that a reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976). In light of the forgoing discussion, the examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a). From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, in the absence of evidence to the contrary, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

NEW GROUNDS OF OBJECTION/REJECTION

Claim Rejections - 35 USC § 112 (1st Paragraph) (New Grounds of Rejection)

Claims 28, 29, 31-48, and 55 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The response filed Apr. 29, 2010 has introduced NEW MATTER into the claims. Amended/new claims 28 and 55 recite a lipid phase consisting of at least one generic crystallizable lipid, at least one generic active principle, and at least one generic stabilizing compound comprising at least two fatty acid chains and one PEG chain. However, written description support is lacking for the broad genus of compositions consisting of this particular combination of ingredients, as is instantly claimed. Nowhere in the originally filed specification is "consisting of" language used to describe any of the phases, let alone the lipid phase. Further, if support could be found in the examples (which applicants did not point to), the specific examples would not support the broad genus of generic compounds instantly claimed. In the absence of support for this broad genus of compositions consisting of the three generic components instantly claimed, the recitations, "...in which the lipid phase consists of at least one crystallizable lipid, at least one active principle, and at least one compound stabilizing compound..." in claims 28 and 55 is new matter and must be removed from the claims.

The response did not point out where support for the "consisting of" language could be found in the originally filed disclosure. Although the PTO has the initial burden of presenting evidence or reasons why persons skilled in the art would not recognize in the disclosure a description of the invention defined by the claims, when filing an amendment an applicant should show support in the original disclosure for new or amended claims. See MPEP 714.02 and 2163.06 ("Applicant should therefore specifically point out the support for any amendments made to the disclosure."). Instant claims 28 and 55 now recite limitations, which were not clearly disclosed in the specification as filed, and now change the scope of the instant disclosure as filed. Such limitations recited in amended claims 28 and 55, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C 112. Applicants are required to provide sufficient written support for the limitations recited in present claims 28 and 55 in the specification or claims, as-filed, or remove these limitations from the claims in response to this Office Action.

Claim Rejections - 35 USC § 112 (2nd Paragraph)

Claims 28, 29, 31-48, and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. In claim 47 the recitation, "...the at least one active principle includes an agent that modifies oral absorption or an enzyme inhibitor." renders the claims indefinite

because it is not clear what the recited agent modifies. Is the agent one that modifies only oral absorption (in which case an enzyme inhibitor is recited as a completely different type of agent) or is it an agent that modifies an enzyme inhibitor as an alternative to modifying oral absorption? The metes and bounds of the claims are unclear.

B. Claims 28 and 55, and all claims dependent thereon are now indefinite because the claim language does not make it clear what the lipid phase must consist of. For example, the claims could be interpreted as requiring an optional thickener and cryoprotective agent in the lipid phase in addition to a crystallizable lipid, an active principle, and a stabilizer. Are the thickener and/or cryoprotective agent in the lipid or aqueous phase? The claim language is ambiguous and the metes and bounds of the claims are unclear. Moreover, no support is found in the specification for the thickener and cryoprotective agent being present in the lipid phase (see p. 9, line 36, and p. 10, line 12). Is this what the claim intends? Thus, the claims could additionally raise the issue of New Matter. However for the purposes of the rejections herein, the claim has been interpreted to mean that the lipid phase consists of at least one crystallizable lipid, at least one active principle, and at least one compound stabilizing the dispersed phase, wherein the optional thickener and cryoprotectant are not necessarily in the lipid phase.

Summary/Conclusion

Claims 28, 29, 31-48, and 55 are rejected; claims 1-27 and 30 are cancelled.

Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kevin S. Orwig whose telephone number is (571)270-5869. The examiner can normally be reached Monday-Friday 7:00 am-4:00 pm (with alternate Fridays off). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sharmila Landau can be reached Monday-Friday 8:00 am-5:00 pm at (571)272-0614. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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